HUMAN SUBJECTS RESEARCH ADVISORY COMMITTEE
Friday, March 9, 2007
CRC Medical Board Room
3:30 p.m.

Present

Dr. Michael Gottesman, Chair
Dr. Howard Austin, NIDDK/NIAMS
Dr. Fabio Candotti, NHGRI
Dr. Robert Conley, NIDA
Ms. Lisa Coronado, RSC
Dr. John Gallin, CRC
Dr. Christine Grady, CRC/DCB
Dr. Maureen Hatch, NCI SS
Dr. Rohan Hazra, NCI
Ms. Charlotte Holden, Acting Exec. Sec.
Dr. Marian Johnson-Thompson, NIEHS
Dr. Barbara Karp, CNS IRB
Dr. Mitchell Max, NIDCR
Dr. Koneti Rao, NIAID
Dr. Robert Shamburek, NHLBI
Mr. Craig Wladyka, IRB Administrator Representative

Absent

Dr. Gilman Grave, NICHD
Dr. Richard Wyatt, OIR
Dr. Susan Olivo-Marsten, FELCOM Representative

Guests

Dr. Lura Abbott, OHSR
Ms. Elaine Ayres, CRC
Ms. Holli Beckerman Jaffe, NEO
Ms. Melissa Bryant, NHLBI
Ms. Laura Cearnal, CC
Ms. Doreen Chaitt, NIAID
Ms. Theresa Doged, OPS
Ms. Bianca Duggins, OPS
Ms. Marjorie Gillespie, NINDS
Mr. Pete Glasz, NIDCR
Ms. Sherri Gollins, NIDCR
Ms. Anne Gupman, NIDA
Ms. Mary Hall, CC
Ms. Donna Howard, NIMH
Dr. Sara Hull, NHGRI
Ms. Kim Jarema, OPS
Ms. Jane Lambert, NIEHS
Ms. Cathy Little, NIAAA
Dr. Jerry Menikoff, OHSR Director Designate (by phone)
Mr. Alex Noury, NINDS
Dr. Suzanne Pursley-Crotteau, NCI
Ms. Jeanne Radcliffe, NIMH
Ms. Kimberley Robinson, OHSR
Dr. Julia Slutsman, NCI
Mrs. Janet Smith. OHSR (Ret.)
Ms. Glynnis Vance, NIDDK
Ms. Victoria Wilitz, NHGRI
Ms. Gretchen Wood, NEI
Dr. Shelia Zahm

1. Minutes of the January 19, 2007 meeting. The minutes were approved without change.

2. Final Version of "A Guide to Preventing Financial and Non-Financial Conflicts of Interest in Human Subjects Research at NIH" (February 2007). Dr. Gottesman said this version is essentially the same as previously reviewed at HSRAC and as previously implemented. It has been approved by Dr. Kington, who made a few minor changes to the wording with advice from legal counsel.

Dr. Gallin said the Patient Advisory Group (PAG) discussed conflict of interest last week. They would like to have the following paragraph added to the consent form as a standard section:

> "**Individual Investigators:** The National Institutes of Health reviews NIH staff at least yearly for conflicts of interest. The following link contains details on this process – http://ethics.od.nih.gov/forms/Protocol-Review-Guide.pdf
> You may ask your research team for additional details or a copy of the Protocol Review Guide."

This wording, written by Ms. Elaine Ayres, has been reviewed by the NIH Ethics Office. Other wording for the consent form that the PAG discussed and approved is similar to what is already in use:

> "The National Institutes of Health and the research team for this study
> (1) have developed (a drug, imaging agent, device) being used in this study. This means it is possible that the results of this study could lead to payments to NIH scientists and to the NIH. By law, government scientists are required to receive such payments for their inventions. You will not receive any money from the development of _____.
>
> "(2) are using (a drug, imaging agent, device) developed by (company name) through a joint study with your researchers and the company. This means it is possible that the results of this study could lead to payments to NIH scientists and to the NIH. By law, government scientists are required to receive such payments for their inventions. You will not receive any money from the development of _____."

PIs and IRBs may modify these last two paragraphs.

Dr. Gottesman pointed out that the NIH has no control over outside investigators. If non-NIH employees are involved in a protocol, language can be added that NIH's conflict of interest rules do not apply to outside investigators.

Dr. Karp asked if the boilerplate consent language could include the paragraph above as well as suitable wording about individual investigators. The HSRAC members were in favor of these suggestions. However, Dr. Gallin pointed out that many protocols do not

have participating outside investigators. It was suggested that the wording could be removed when inappropriate or it could be made conditional. Dr. Gottesman promised that boilerplate language would be developed.

There was discussion about the sentence in the last paragraph of section V of the "Guide" which states that ". . . new NIH policy will require that the informed consent document signed by protocol participants contain a statement that one or more investigators own a de minimis amount of stock in the company that makes the product being tested in the protocol." Dr. Hazra said he receives many queries about *de minimis* holdings, including the amount below which the government requires disclosure. Ms. Beckerman Jaffe responded there are three levels of *de minimis* holdings: $15,000, $25,000 and $50,000, depending upon whether the holdings are in companies directly involved with a protocol, companies that are in the same field as the company sponsoring a protocol, or sector mutual funds. She reminded the group that financial disclosure of even a very minor amount may be required in journal publications.

The DECs know when there are *de minimis* stock holdings and certify either that there is no conflict or that the conflict has been resolved. A conflict may be identified even when there is only a *de minimis* holding. Dr. Max urged clarification for the IRBs and suggested the DECs should let the PIs and Chairs know when there ought to be a comment in the consent form about individual holdings. Ms. Ayres said that DEC will note if a participant in a study holds stock in a drug under investigation.

Dr. Hatch asked who is supposed to handle an above *de minimis* conflict of interest which recently came to her attention. Ms. Ayres said the conflict should have been resolved before coming to the IRB. Dr. Hazra agreed that a clear message to IRB Chairs is important, and noted that the NCI DEC has been certifying "waiver" on some COI forms. He would like boilerplate language to be provided regarding disclosure of holdings of *de minimis* amounts of stock. Ms. Ayres agreed to draft such language for review by NIH ethics leadership.

Dr. Gallin concluded that patients only want to know that any conflict of interest issue is being handled, and Dr. Grady agreed that the majority of patients are not interested in the details of stock ownership.

3. Combined Neurosciences (CNS) IRB. Dr. Karp said that the CNS is now fully combined, and is meeting as two panels. NEI was included in January. Normally, protocols are reviewed by the panel with the appropriate expertise and remain with that panel for subsequent continuing reviews. Protocols requiring no special expertise go to the panel with the next available meeting. There are currently approximately four hundred protocols under review, mostly physiological studies and clinical trials, covering a wide range of diseases. Two four-hour meetings are held each month, and expedited reviews are done whenever possible, with the assistance of IRB members and a final decision by Dr. Karp. A retreat was held in February which discussed administrative topics in the morning and other IRB issues in the afternoon, such as phase I trials

risk/benefit assessments, etc. The retreat minutes are being finalized and will be distributed to anyone who is interested.

Dr. Gottesman said that it is important to acknowledge in some way the service of former IRB members whose Institute IRBs are now part of the CNS. He asked Dr. Karp whether the CNS would consider reviewing other neuroscience protocols. Dr Karp said this is already done occasionally, e.g., for the Clinical Center, but the workload would not permit any more protocols unless additional staff were hired. Dr. Gottesman commented that the CNS model will be carefully observed over time.

4. FWA and IRB Membership. Dr. Abbott said that a mandatory training session had just been held for the IRB Administrators about IRB membership and IRB membership lists. A requirement of the NIH Federal Wide Assurance (FWA) is that all NIH IRBs are registered with the Office of Human Research Protections (OHRP). OHRP pays close attention to the constitution of the IRBs to make sure that the expertise is balanced and appropriate for the protocols being reviewed. Day-to-day management of the rosters is important because if OHRP conducted an NIH site visit, OHRP would carefully examine the IRB minutes, rosters and appointment letters.

OHSR is responsible for communicating the details of the NIH FWA to OHRP, but cannot do so unless it receives up-to-date information from the IRBs. This includes requests to Dr. Gottesman for appointment of new members from the Scientific and Clinical Directors, with details of the roles of these new members on the IRB, and, particularly important, notice of when members leave the IRB.

Last week OHSR sent to OHRP updated lists of all the NIH IRBs, and registered the two new panels of the CNS, so for the time being, the NIH FWA is up to date for IRBs and IRB members. Dr. Abbott requested that OHSR be apprised of any changes as they occur.

5. Human Biospecimen Tracking and Storage at NIH. Before Dr. Shelia Zahm gave her presentation about human biospecimen tracking and storage at NIH to HSRAC, Dr. Gottesman noted that the new NIH Reform Act of 2006 requires annual reports to Congress on how NIH stores and tracks human tissue samples. As a result of Congressional hearings in June, 2006, Dr. Gottesman and the Scientific Directors (SDs) set up an *ad hoc* SD's Subcommittee on Biorepository Practices and Guidelines within the Intramural Research Program. This Subcommittee is co-Chaired by Dr. John Gallin and Dr. Shelia Zahm, NCI. The Subcommittee has broad expertise and representation by Institute.

The overall goals of the Subcommittee are to ensure that NIH handles biospecimens according to the highest ethical and scientific standards; to maintain the public's trust; to preserve and protect biospecimens and the substantial investment that they represent, and to facilitate research by maximizing use of the specimens.

Specifically, the Subcommittee will determine the scope and current conditions of biospecimen storage in the IRP; identify steps needed to meet "best practices" guidelines for biospecimen storage; evaluate use of local harmonized biorepositories *vs*. creation of a centralized facility, including resource requirements; evaluate inventory tracking systems that can be used to manage biospecimen collections and meet reporting requirements, and consider implementation for new specimen collections *vs* legacy collections. Dr. Zahm noted that there is an optimistic time frame of six months for completion of the subcommittee's work.

Last month, the Laboratory and Branch Chiefs were sent a questionnaire about the status of biospecimen storage and existing biospecimen inventory tracking systems in the IRP. The response to this survey has been excellent. The Subcommittee is also assessing other biospecimen inventory tracking systems in order to provide information to Scientific Directors who are considering systems for their Institutes and to gather data for development of a RFP for a centralized system, should that be the eventual recommendation of the Subcommittee. NCI has already developed a system and there are some integrated systems available, but the subcommittee will not dictate any particular system.

Dr. Zahm acknowledged that the subcommittee's focus is on prospective biospecimens rather than legacy collections because it is not feasible to upgrade inventory and track existing collections. It would, however, be useful to find out what the IRBs need to know about existing collections in order to track them properly.

The Subcommittee is also evaluating the case for a centralized storage facility on or near the NIH campus and should have information on this by April or May. Dr. Zahm said that storage space can now be minimized by the use of new and more efficient techniques.

Dr. Gottesman said it is not yet clear what the final product will be. However, donors will continue to agree in consents to specific circumstances for the acquisition, storage and disposition of their specimens. Boilerplate language could be developed for this.

Dr. Gottesman was asked how Material Transfer Agreements apply to biorepositories. He said that a review by an IRB or OHSR is required for specimens shipped outside NIH, and a determination has to be made of whether additional consent is needed or whether the original consent suffices. Help and support from the technology transfer professionals will be needed for this complicated issue, and Dr. Rohrbaugh is completing the guidance he presented to HSRAC last month. Dr. Gallin observed that if specimens cross a state line, an MTA is needed. It was questioned whether or not this rule applies to NIH components out of state.

Dr. Zahm was asked if repositories will include data. She said that repositories are for specimens only, i.e., any sample linked to a person, rather than data. Incoming specimens from outside NIH, regardless of the mechanism by which they were obtained, will be covered. Once specimens are received here, the responsible investigator has

stewardship of them. She said that DNA samples are viewed as specimens, but not cloned DNA or cell lines. (Note: This applies to cloned DNA or cell lines that are publicly available - See *Guidelines for the Conduct of Research at NIH*, page 4, Section *B.)*

Dr. Hatch said the template language relating to samples does not regulate the recipient of the samples. Dr. Gottesman agreed that this point needs clarification, and said it will eventually be dealt with.

Dr. Gallin commented that he hoped that it would be possible to link any future biorepository samples, including phenotype/genotype information, to the clinical research information system and the protocol from which it was obtained.

Dr. Gallin praised Dr. Zahm for her work on the subcommittee. Dr. Gottesman said that her presentation was for information only for the time being.

There were no announcements or information items. The meeting closed at 4:45 p.m. The next meeting will take place on May 11, 2007.